Multiple Organ Infarctions Following Disseminated Intravascular Coagulation Precipitated by Sepsis in a Healthy Infant: A Case Report

Chien-Hua Wang,[1,2] Min-Sheng Lee,[1] Lung-Chang Lin,[1,2] and Rei-Cheng Yang[1,2]
[1]Department of Pediatrics, Kaohsiung Medical University Hospital, and [2]Graduate Institute of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan.

Multiple organ infarctions are a very rare clinical event in children. We report a 3-month-old infant with sepsis and disseminated intravascular coagulation, who was diagnosed with cerebral ischemic stroke associated with middle cerebral artery stenosis and subsequent retinal infarction by magnetic resonance imaging, fundoscopy and magnetic resonance angiography. In addition, he suffered from renal infarction with hypertension and was treated until 1 year of age. We emphasize the importance of early recognition of organ infarctions, prophylaxis of risk factors and of optimized therapy of the underlying etiology.

Key Words: disseminated intravascular coagulation, infant, multiple organ infarction
(*Kaohsiung J Med Sci* 2010;26:663–8)

Disseminated intravascular coagulation (DIC) is characterized by inappropriate widespread activation of coagulation that leads to extensive microvascular thrombosis and hemorrhage. It is not a rare disorder, and has a frequency of 1.12% in hospitalized children, especially in those with sepsis [1]. Septic patients with severe DIC might present with manifestations of thromboembolic disease or with clinically less apparent microvascular fibrin deposition, which presents predominantly as multiple organ dysfunction [2]. Bleeding is the leading clinical symptom [1]. However, macrocirculatory thrombotic events are rare in this setting, except in babies who have a central catheter *in situ*. We report on the case of a 3-month-old previously healthy Taiwanese infant, who presented with multiple organ infarctions, including brain, retina, kidney and skin, following septic shock and DIC.

Case Presentation

A previously healthy 3-month-old male infant presented to our emergency department with altered consciousness, and was admitted to the pediatric intensive care unit under suspicion of sepsis. Five days earlier, fever and poor feeding, with clinical signs of upper respiratory tract infection, were noted, followed by diarrhea with muddy and mucus-coated stool 2 days later, when plain abdominal X-ray and abdominal echography revealed no specific findings. On the following 2 days, he was noted to have multiple petechial rashes over the chest and abdomen, with bloody stools.

On admission, the infant appeared irritable and ill. He had dyspnea and unstable vital signs, with a respiratory rate of 40 breaths/min, pulse rate of 220 beats/min and blood pressure of 36/17 mmHg. On physical examination, he showed lip cyanosis, dry oral mucosa

Received: Mar 5, 2010 Accepted: Apr 27, 2010
Address correspondence and reprint requests to: Dr Rei-Cheng Yang, Department of Pediatrics, Kaohsiung Medical University Hospital, 100 Shih-Chuan 1st Rd., Kaohsiung 807, Taiwan.
E-mail: rechya@kmu.edu.tw

and mottled skin. Respiratory distress with subcostal retraction and nasal flaring was evident. His extremities were cold, with a prolonged capillary refilling time. Laboratory examination revealed a white blood cell count of 31,000/μL; platelet count of 623,000/μL; serum creatinine, 1.0 mg/dL; blood urea nitrogen, 23.8 mg/dL; C-reactive protein, 9.8 mg/L; prothrombin time, 16.3 seconds (normal range, 8.0–12.0 sec); activated partial thromboplastin time, 38.5 seconds (normal range, 24.0–36.8 sec); and D-dimer, 5,777 μg/L (normal range, <324 μg/L). Liver enzymes were elevated [aspartate aminotransferase = 4,047 IU/L (normal range, 10–42 IU/L); alanine aminotransferase = 1,424 IU/L (normal range, 10–40 IU/L)] and blood lactate level was 12.9 mmol/L (normal range, 0.5–2.2 mmol/L). Stool routine showed 2+ occult blood; urine analysis revealed hematuria (5–10 red blood cells/high power field) and 4+ proteinuria. Chest radiographs were normal. Septic shock with multiple organ dysfunction (liver dysfunction, coagulopathy and prerenal azotemia) and metabolic acidosis (venous blood gas = pH 7.2; partial pressure of CO_2 = 11 mmHg; HCO_3^- = 6.3 mmol/L) were observed. Blood cultures were obtained, and intravenous cefotaxime and ampicillin were initiated. The patient was managed with fresh frozen plasma on day 1 and mechanical ventilation and the vasopressor dopamine for 1 day.

On day 2, however, right focal seizure occurred and hypertension (150/90 mmHg) and frequent apnea were noticed. Magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) indicated acute infarction in the right fronto-temporo-parietal lobe and basal ganglia in the right middle cerebral artery (MCA) territory, and complete occlusion of the internal carotid artery (Figures 1 and 2A). Lumbar puncture showed clear cerebrospinal fluid without pleocytosis.

On day 3, enlarged, well-demarcated, purplish black areas of hemorrhagic cutaneous necrosis and discoloration of the patient's left toes and fingers were noticed (Figure 3). Prothrombotic status was indicated, based on protein C and protein S deficiency, with serum levels of 30% (normal range, 80–132%) and 88% (normal range, 55–130%), respectively; prothrombin time of 19.7 seconds with international normalized ratio = 1.99; activated partial thromboplastin time of 36.6 seconds; fibrinogen, 141 mg/dL (normal range, 170–410 mg/dL); and antithrombin III, 44% (normal range, 85–118%). Platelet count continuously dropped in the following 3 days from 124,000/μL to 33,000/μL. Transthoracic echocardiography showed no vegetation or embolism. Vancomycin was initiated in addition to cefotaxime due to progression of DIC and sepsis.

On day 5, anisocoria occurred. On fundoscopic examination, whitening and edematous retina with exudate and hemorrhage, as well as signs of the retina folding over the macular area, were found, which were compatible with retinal infarction caused by central retina artery occlusion (CRAO). Furthermore, hypertension (120/80 mmHg) was noted when dopamine was tapered off. In addition, proteinuria and hematuria persisted. Elevated plasma renin level was detected at

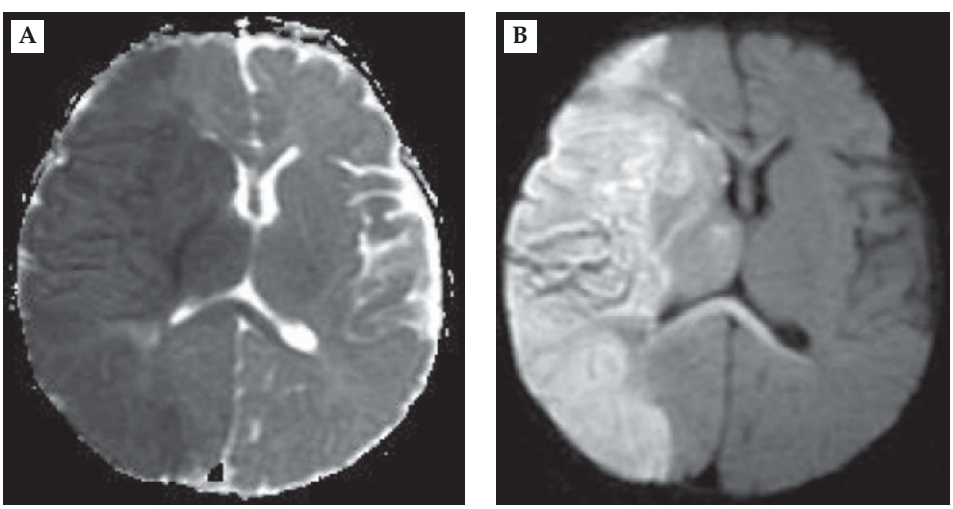

Figure 1. *Age 3 months. (A) Apparent-diffusion-coefficient image and (B) diffusion-weighted axial magnetic resonance image demonstrated low and high signals in the right middle cerebral artery and partial posterior cerebral artery territory, with midline shift to the left side, which suggested acute infarction.*

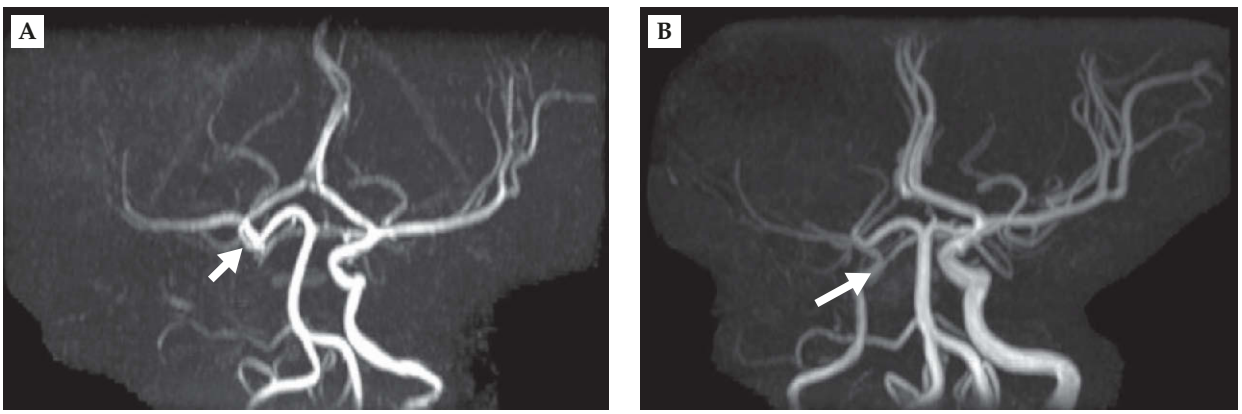

Figure 2. *(A) Age 3 months. Magnetic resonance angiography showed absence of the right internal carotid artery. Suspected obstruction at the internal carotid-posterior communication (IC-PC) level with collateral circulation from the opposite side. (B) Age 1 year and 7 months. Magnetic resonance angiography showed stenosis of the right internal carotid artery and occlusion of most of the branches of the right middle cerebral artery.*

Figure 3. *Extensive ecchymoses and purpuric skin rash with discoloration of the toes.*

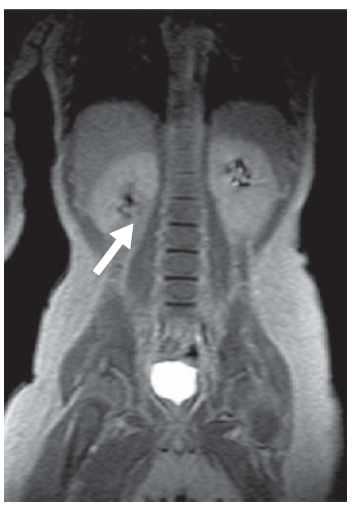

Figure 4. *Magnetic resonance imaging of the abdomen. T1-weighted images showed a focal, relatively hypointense area at the lower pole of the right kidney, with poor enhancement. A focal cortical retraction adjacent to this lesion was also noted.*

>330.0 pg/mL. An MRI of the abdomen suggested focal infarction at the lower pole of the right kidney (Figure 4).

Cerebrospinal fluid and blood culture were negative, while urine culture showed growth of *Klebsiella pneumoniae*. We gave the patient additional supportive therapy, including fresh frozen plasma and platelets. There was a significant improvement in the patient's skin lesions and areas of impending gangrene, including his left toes and fingers, as well as drug control of hypertension. Coagulation function parameters all returned to within normal limits, including protein C and antithrombin III, with serum levels of 94% and 114%, respectively. Follow-up fundoscopic examination showed right optic nerve atrophy.

Five weeks after admission, the patient was discharged with left spastic hemiplegia and visual deficit. Under regular follow-up, hypertension improved and antihypertensive drugs were tapered at the age of 1 year. Subsequent MRI and MRA at the age of 1 year and 7 months revealed encephalomalacia in the right MCA territory and left frontal lobe, as well as stenosis of the right internal carotid artery (Figures 2B and 5)

Discussion

Our patient initially presented with systemic inflammatory response syndrome that was triggered by upper respiratory tract infection and acute enteritis. He also presented with multiple organ dysfunction.

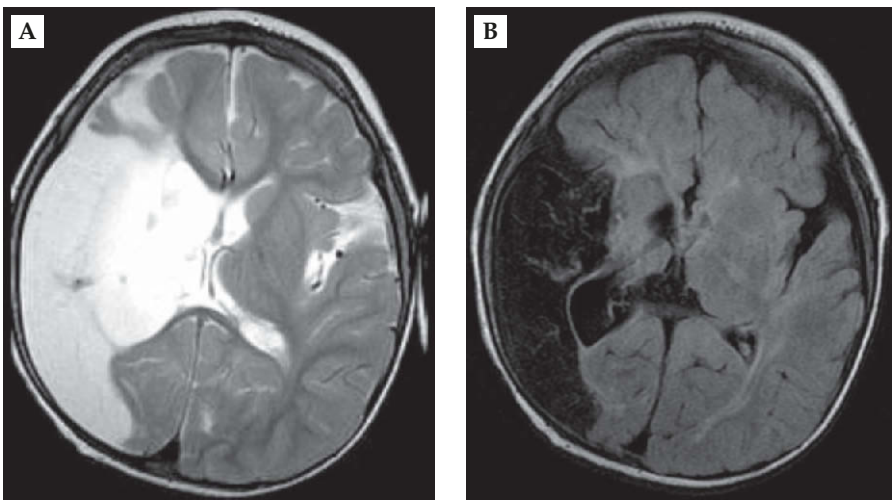

Figure 5. *Magnetic resonance image of the patients at the age 1 year and 7 months. (A) T2-weighted image and (B) T2 FLAIR demonstrated encephalomalacia in the right middle cerebral artery territory and left frontal lobe.*

Therefore, severe sepsis was suspected. Besides, he showed manifestations of thrombosis, predominately with multiple organ infarctions that involved the brain, ocular globe, acral skin and kidney. The prothrombotic condition was transitory because all of the coagulation parameters ultimately returned to normal values. It was clear that acquired protein C and antithrombin III deficiencies were associated with sepsis. It is widely assumed that dehydration predisposes to venous thromboembolism [3]. Briefly, multiple organ infarctions are a very rare clinical event. To the best of our knowledge, this is the first reported case of multiple organ infarctions in the setting of transitory coagulation dysfunction.

Pediatric stroke is a rare clinical event and occurs at a rate of 2–3 per 100,000 children per year [4]. The presence of neurological deficits is about 50% [5]. Infants have a higher rate of ischemic stroke, especially arterial ischemia stroke (AIS) [6]. Clinically, children aged < 1 year with cerebral AIS are more likely to present with epileptic seizures and altered mental status [7]. In addition, Lee et al reported that multiple risk factors of AIS in children could be identified, including prothrombotic state, vasculopathy and infection [8]. For instance, our patient manifested with a hypercoagulation state and hyperviscosity caused by hypovolemia and hypoperfusion, which might have contributed to total occlusion of the right MCA at initial presentation. Furthermore, brain MRA at the age of 1 year and 7 months revealed vasculopathy with stenosis of the right MCA. A previous study has demonstrated that acute intracranial stenoses can be formed, at least in part, by mobile thrombi, and the degree of stenosis decreases during follow-up [9]. However, the intracranial vasculopathy is associated with a high recurrent rate of stroke [10].

Retinal infarction due to CRAO is a rare clinical event with an incidence of approximately 1–10 in 100,000 [11]. Visual acuity in patients with CRAO is poor at presentation, and prognosis is generally poor, as in our patient [12]. It has been reported that cerebral microembolisms are frequent in patients with symptomatic retinal embolism, and are associated with internal carotid artery stenosis in > 50% of cases [13]. As in our patient, AIS results from thrombosis-induced occlusion of the right MCA, followed by ipsilateral retinal infarction. Clinically, our patient presented with anisocoria and sluggish ocular movement in response to light, which are acute clinical features of CRAO. Owing to the subtle signs at presentation in a sick baby with stroke, it is important for clinicians to keep retinal infarction in mind in such patients with AIS, to make an early diagnosis.

Renal infarction is rare and difficult to recognize because of its nonspecific presentation and its rarity. More than half of patients with renal infarction present with microscopic hematuria and proteinuria [14]. Concurrent thromboembolism in other foci, which has a prevalence of 37%, should be noted, and early imaging should be considered for high-risk patients. In our patient, due to early diagnosis and appropriate management, the outcome was good.

In our patient, anticoagulation therapy was not performed, with complete recovery from renal infarction, arcal ischemia and skin infarction lesions; treatment was aimed to correct the underlying conditions and provide supportive treatment for DIC [2]. However, as far as AIS is concerned, the American College of Chest Physicians and United Kingdom Guidelines have suggested antithrombotic and anticoagulant drugs in acute childhood AIS [15]. These guidelines remain controversial because none of the treatment recommendations have been derived from randomized clinical trials [16]. Second, less than half of children with AIS do not have their stroke radiologically confirmed until >24 hours after clinical onset [14]. This makes it difficult to establish guidelines for thrombolytic therapies for children [17]. Therefore, it is suggested that anticoagulation therapy should be reserved for cases in which the onset of AIS is not certain, and further hemorrhage is highly predicted.

In conclusion, multiple organ infarctions related to thromboembolism after septic shock is a rare event in children. Early recognition and prophylaxis of risk factors, as well as optimized therapy of underlying etiology are of the greatest importance.

References

1. Oren H, Cingoz I, Duman M, et al. Disseminated intravascular coagulation in pediatric patients: clinical and laboratory features and prognostic factors influencing the survival. *Pediatr Hematol Oncol* 2005;22: 679–88.
2. Levi M, Ten Cate H. Disseminated intravascular coagulation. *N Engl J Med* 1999;341:586–92.
3. Kelly J, Hunt BJ, Lewis RR, et al. Dehydration and venous thromboembolism after acute stroke. *Q J Med* 2004;97:293–6.
4. Lynch JK, Hirtz DG, deVeber G, et al. Report of the National Institute of Neurologic Disorders and Stroke Workshop on Perinatal and Childhood Stroke. *Pediatrics* 2002;109:116–23.
5. Lanthier S, Carmant L, David M, et al. Stroke in children: the coexistence of multiple risk factors predicts poor outcome. *Neurology* 2000;54:371–8.
6. Carvahlo KS, Garg BP. Arterial strokes in children. *Neurol Clin* 2002;20:1079–100.
7. Zimmer JA, Garg BP, Williams LS, et al. Age-related variation in presenting signs of childhood arterial ischemic stroke. *Pediatr Neurol* 2007;37:171–5.
8. Lee YY, Lin KL, Wang HS, et al. Risk factors and outcomes of childhood ischemic stroke in Taiwan. *Brain Dev* 2008;30:14–9.
9. Diehl RR, Samii C, Diehl A. Dynamics and embolic activity of symptomatic intra-cranial cerebral artery stenoses. *Acta Neurol Scand* 2002;106:173–81.
10. Strater R, Becker S, Eckardstein AV, et al. Prospective assessment of risk factors for recurrent stroke during childhood—a 5-year follow-up study. *Lancet* 2002;360: 1540–5.
11. Rumelt S, Dorenboim Y, Rehany U. Aggressive systematic treatment for central retinal artery occlusion. *Am J Ophthalmol* 1999;128:733–8.
12. Yuzurihara D, Iijima H. Visual outcome in central retinal and branch retinal artery occlusion. *Jpn J Ophthalmol* 2004;48:490–2.
13. Wijman CA, Gomes JA, Winter MR, et al. Symptomatic and asymptomatic retinal embolism have different mechanisms. *Stroke* 2004;35:e100–2.
14. Srinivasan J, Miller SP, Phan TG, et al. Delayed recognition of initial stroke in children: need for increased awareness. *Pediatrics* 2009;124P:e227–34.
15. Monagle P, Chan A, Massicote P, et al. Antithrombic therapy in children. Seventh ACCP Conference on Antithrombic and Thrombolytic Therapy: Evidence-Based Guidelines. *Chest* 2004;126:645S–87S.
16. deVeber G. In pursuit of evidence-based treatments for paediatric stroke: the UK and Chest guidelines. *Lancet Neurol* 2005;4:432–6.
17. Mallick AA, Ganesan V. Arterial ischemic stroke in children–recent advances. *Indian J Pediatr* 2008;75:1149–57.

瀰漫性血管內凝血病變與敗血症伴隨多發性器官梗塞的健康嬰兒：病例報告

王建華[1,2] 李敏生[1] 林龍昌[1,2] 楊瑞成[1,2]

[1]高雄醫學大學附設醫院 小兒科

[2]高雄醫學大學 醫學研究所

臨床上，孩童發生多重性器官梗塞是很罕見的。以下報告一個年紀 3 個月嬰兒發生瀰漫性血管內凝血病變與敗血症，透過臨床、腦部核磁共振與血管攝影、眼底鏡檢查，同時被診斷為與中大腦動脈硬化相關的大腦缺血性中風合併視網膜的梗塞。此外，個案同時也有腎臟梗塞並有高血壓併發症，一直到 1 歲之前，都需要藥物治療的控制。我們強調器官梗塞的早期發現、危險因子的預防並且針對致病病因給予最佳治療是極具重要性的。

關鍵詞：瀰漫性血管內凝血病變，嬰兒，多重性器官梗塞

（高雄醫誌 2010;26:663–8）

收文日期：99 年 3 月 5 日

接受刊載：99 年 4 月 27 日

通訊作者：楊瑞成醫師

高雄醫學大學附設醫院小兒科

高雄市三民區十全一路 100 號